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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/037,299	10/25/2001	Stewart Thomas Leslie	208.1009	4506

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Davidson, Davidson & Kappel, LLC
485 7th Avenue
14th Floor
New York, NY 10018

EXAMINER	
YOUNG, MICAH PAUL	
ART UNIT	PAPER NUMBER
1618	
MAIL DATE	DELIVERY MODE
10/21/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/037,299	LESLIE, STEWART THOMAS	
	Examiner	Art Unit	
	MICAH-PAUL YOUNG	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 August 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 5-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 5-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/21/09 has been entered.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1, 2, 5-13, 16, 18, 20, 21 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Lee (WO 90/04965 hereafter referred to as '965).

3. The '965 patent teaches a transdermal preparation and device comprising opioid analgesics and opioid antagonists. The antagonist negates the analgesic properties of the opioid if the dosage form is delivered via bolus injection or oral delivery (abstract). The antagonist is not permeable through the skin in the transdermal presentation, and is incorporated with the same vehicle of the opioid analgesic (abstract). The transdermal device comprises an aqueous alcohol environment (example), a release liner and a backing layer (figures). The drugs listed as useful in the invention include fentanyl, buprenorphine butorphanol, cocaine and methadone (pg. 4, lin. 14 – 20). Antagonists include naltrexone (pg. 4, lin. 21-25). Naltrexone is well known as

nauseants in opioid formulations and has severe side effects including severe headache, body ache, vomiting and nausea. The device can be either a reservoir or a monolithic patch (figures). These disclosures render the claims anticipated.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 2, 5-13, and 15-23 rejected under 35 U.S.C. 103(a) as being unpatentable over the combined disclosures of Lee (WO 90/04965 hereafter referred to as '965) in view of Blum et al (USPN 5,891,919 hereafter '919), Porter (USPN 4,175,119 hereafter '119). The claims are drawn to a transdermal formulation comprising an opioid analgesic such as buprenorphine and distressing agents such as an ergolide, bitter quaternary ammonium compounds or an emetic compound.

4. As discussed above the '965 patent discloses a transdermal patch formulation where an abusable opioid can be delivered and an opioid antagonist useful in deterring abuse is present in the patch yet is not permeable through the skin. The antagonist causes nausea, vomiting and headaches when digested orally. The reference is silent to the specific deterring compound of the instant claims however. These compounds are well known in the art and it would have been obvious to include them into the '965 patent.

5. The '919 patent discloses a formulation comprising denatonium capsaicinate as a substance providing a bitter and/or spicy flavor for use as an aversive agent (Abstract). It may be incorporated into topical formulation and dressings and other pharmacological compositions (See Column 4, Lines 38-47). It would have been obvious to include the compound into the '538 formulation since this reference establishes the compounds use in aversion technologies.

6. The '119 patent discloses the use of an emetic to prevent accidental or intentional overdose of a psychoactive substance (Abstract, Column 1, lines 40-43). Such emetic substances include emetine hydrochloride, ipecamine, hydro-ipecamine and ipecacuanhin acid (Column 1, lines 52-57). It may be incorporated into formulation containing narcotic analgesics such as hydromorphone and codeine (Column 3, Lines 55-57). It would have been obvious to include the emetics into the '538 patent since both reference disclose the control of misusing the same compounds.

7. It would have been obvious to combine the bitter and emetic compounds of the '919 and '119 patents in order to provide a sufficient deterrent to potential misuse. The '965 patent discloses a transdermal formulation comprising opioid analgesics along with compounds that prevent abuse by ingestion or solvent extraction. These compounds included nauseants such as

naloxone. The reference establishes the level of skill in the art regarding the inclusion of nauseants and distressing compounds into potential abusive compositions. The bitter/spicy flavoring compounds of the '919 would cause distress if applied directly, and the emetics of the '119 would cause nausea upon exposure. It would have been obvious to combine the compounds in the transdermal formulation of the '965 with an expected result of a transdermal formulation useful in deterring misuse.

8. Claims 1, 2, 5-16, 18 and 20-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined disclosures of Lee (WO 90/04965 hereafter '965) in view of Yum et al (USPN 6,001,390 hereafter '390) and Drugs: Facts and Comparisons, entry for *Pergolide Mesylate* pages 1621-1624.

9. As discussed above the '965 patent discloses a transdermal patch formulation where an abusable opioid can be delivered and an opioid antagonist useful in deterring abuse is present in the patch yet is not permeable through the skin. The antagonist causes nausea, vomiting and headaches when digested orally. The reference is silent to the specific deterring compound of the instant claims however. These compounds are well known in the art and it would have been obvious to include them into the '965 patent.

10. The '390 patent a transdermal formulation comprising pergolide salts (abstract). The pergolides do not readily permeate through the skin and require permeation enhancers (col. 4, lin. 47-65). It would have been obvious to include the pergolide into the transdermal formulation of the '538 since they are similar formulations with similar components.

11. According to the *Pergolide* entry in the Drug textbook, the most common adverse reactions include nausea, dyskinesia, somnolence and rhinitis (page 1622). An artisan of

ordinary skill would have been motivated to include the pergolide into the transdermal formulation of the '538 patent since the common side effects would negatively impact a user upon misuse. Since the pergolides would not be permeable through the skin, they would act to deter misuse through injection or solvent distillation.

12. With these things in mind it would have been obvious include the ergot compounds of the '390 patent into the misuse deterring transdermal formulation of the '538 patent in order to provide sufficient deterrents to misuse. The side effects of pergolide salts are well known in the art as shown in the Drug textbook, and would have been an obvious addition to an aversion formulation. It would have been obvious to combine the teachings and formulations with an expected result of a transdermal formulation useful in treating pain without leading to potential abuse.

Response to Arguments

Applicant's arguments filed 8/21/09 have been fully considered but they are not persuasive. Applicant argues that:

The Lee reference does not anticipate the instant claims since the claims are free of non-permanent opioid antagonists and these are required by the Lee patent.

Regarding this argument it remains the position of the Examiner that the Lee patent anticipates the instant claims. The claims have been amended to remove non-permanent opioid antagonist from the device, and the Lee patent discloses the use of naloxone and its salts as possible antagonist. The instant specification defines non-permanent opioid antagonist as naloxone and its salt. However the Lee patent also discloses the use of naltrexone (page 5, lin. 16). Naltrexone is not a salt or derivative of naloxone and thus is not excluded by the new

amendment. Naltrexone is an opioid antagonist that can cause nausea, vomiting and headaches. As such the Lee patent continues to teach a transdermal device comprising an opioid analgesic and an opioid antagonist that causes distress to the user when delivered. For these reasons the claims remain anticipated.

The combination of the Lee, Blum and Porter patents does not obviate the instant claims since there woudl be no motivation to combine the distressing compounds of the Blum and Porter patents into the formulation of the Lee patent.

Regarding this argument, it remains the position of the Examiner that it would have been obvious to substitute the distressing compounds of the Blum and Porter patents into the formulation of the Lee patent since each compound causes the same distress deterring the user from misuses. Each of the compounds in the Lee, Blum and porter patents solves the same problem, namely deterring misuse of opioid analgesic. Each distressing compound causes nausea, vomiting and headaches when used. Since each compounds substituted into the formulation would salve the same problem of deterring opioid misuse, it woudl have been obvious to substitute the compounds into similar formulations, despite the differing mechanisms of action. As stated above the Lee patent discloses the use of naltrexone, an opioid antagonist that despite the amendment continues to be useable in the instant claims. For these reasons the claims remain obviated.

The combination of the Lee patent with the Pergolide drug entry would not obviate the instant claims since there would be no motivation to combine the references.

As discussed above the Lee patent, despite the amendment foreclosing the use of naloxone, continues to disclose the use of a different and distinct opioid antagonist naltrexone

that is not foreclosed or excluded by the instant claims. The claims require the distressing compound to cause nausea which naltrexone does; as such the Lee patent continues to obviate the claims. Since compounds that cause nausea, headaches and vomiting are useful in the Lee patent, the substitution or inclusion of pergolide woudl have been an obvious modification since these compounds woudl solve the same problem of deterrence. For these reasons the claims remain obviated by the combination of the Lee and Drug facts entry.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICAH-PAUL YOUNG whose telephone number is (571)272-0608. The examiner can normally be reached on Monday-Friday 8:00-5:30; every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

/MICAH-PAUL YOUNG/
Examiner, Art Unit 1618